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September 17, 200 1

The Honorable Christine Todd Whitman
Administrator
U.S. Environmental Protection Agency
Ariel Rios Building
Room 3000, #1101-A
1200 Pennsylvania Ave., N.W.
Washington, DC 20460

Subject: Comments on HPV Test Plan and Robust Summaries for the Alkylphenols Category

Dear Administrator Whitman:

The following comments on the test plan for the alkylphenols category are submitted on behalf of the Physicians Committee for Responsible Medicine, People for the Ethical Treatment of Animals, the Humane Society of the United States, the Doris Day Animal League, and Earth Island Institute. These health, animal protection, and environmental organizations have a combined membership of more than nine tnillion Americans. We again request a response from the Environmental Protection Agency (EPA) to these comments as we have yet to receive a response to any of the 26 test plan comments we have submitted to date over the past year.

We applaud Schenectedy International's efforts in building a category of logically related chemicals with similar structure and functional groups. Importantly, they have identified trends in the association between chemical properties and toxicity, and have used these trends to predict toxicological hazard potential of members of the category.

We agree that no further testing on animals is necessary. Additional animal tests would not contribute to **the** understanding of the alkylphenols' impact on human and ecological health. Moreover, these substances are irritating and corrosive, and any further testing would violate animal welfare guidelines.

Our three concerns **with** the test plan are:

1. The EPA needs to ensure inter-industry cooperation in the development of chemical categories and test plans.
2. The HPV program lacks the mechanism for bringing forth data that would contribute more to the understanding of chemical hazards than the crude SIDS battery.
3. Given the irritating and corrosive nature of these substances, any testing on animals is inappropriate under animal welfare guidelines.

1. **The EPA needs to ensure inter-industry cooperation in the development of chemical categories and test plans.**

While Schenectedy International has identified 17 compounds to include in its category, we have identified at least 15 additional HPV chemicals that could be incorporated into this group. These additional HPV chemicals

are listed in Table 1.

As previously discussed in other test plan comments, such as our comments on the American Petroleum Institute Petroleum Coke test plan, the Phosphite Producers HPV Consortium test plan on tris (nonylphenol)phosphite, and the General Electric test plan on p-cumylphenol, we are concerned that the EPA is not encouraging inter-company and inter-industry cooperation in development of test plans and chemical categories. Therefore, many chemicals that could be easily included in this group are not being evaluated. In fact, many structurally similar chemicals remain unsponsored under the HPV program. Inclusion of these additional compounds in the alkylphenols category would result in a cheaper, more efficient analysis of chemicals, and would reduce the number of animals killed in this program. We would like to know how the EPA is addressing our concerns on this issue as well as encouraging inter-industry cooperation. At this point, we have received absolutely no response from the EPA on this issue, nor have we received a response to the 26 test plan comments submitted to date.

Schenectedy International has developed a thoughtful analysis of how various physicochemical properties affect potential toxicity. For example, the company has demonstrated that K_{OW} correlates well with measured aquatic toxicity of these compounds. It has identified similar trends with molecular weight, solubility, and vapor pressure. However, the EPA should provide the support for this analysis to include additional structurally and toxicologically similar chemicals.

2. **The HPV program lacks the mechanism for bringing forth data that would contribute more to the understanding of chemical hazards than the crude SIDS battery.**

Alkylphenol compounds are used mainly as intermediates in the synthesis of primary and secondary antioxidants, demulsifiers, surfactants, lube oil additives, biocides, fragrances, inks, and resins. They may also be used as polymerization inhibitors, epoxy resin hardeners, heat stabilizers, and polycarbonate chain terminators. Existing in vivo and in vitro studies are available on the metabolism, environmental fate, and transport of these chemicals, as well as toxicity of the alkylphenols.[1-7]

3. **Given the irritating and corrosive nature of these substances, any testing on animals is inappropriate under animal welfare guidelines.**

The extensive studies on alkylphenols indicate they are of low acute systemic toxicity, but are known to be irritating or even corrosive to the skin and/or eyes. Any further testing would be inappropriate and cruel.

Thank you for the opportunity to comment. We would greatly appreciate a response from the EPA, indicating that it is taking these comments into account and is requiring compliance with the standards of the HPV program and the October 1999 letter. I can be reached at 202-686-2210, ext. 302, or via e-mail at <ncardello@pcrm.org>. Correspondence should be sent to my attention at the following address: 5 100 Wisconsin Ave., N.W., Suite 400, Washington, DC 20016. I look forward to your response on this important issue.

Sincerely,

Nicole Cardello, M.H.S.
Staff Scientist

References

1. Gutendorf B, Westendorf J. Comparison of an array of in vitro assays for the assessment of the estrogenic potential of natural and synthetic estrogens, phytoestrogens, and xenoestrogens. Toxicology 2001; 166(l-2):79-89.

2. lnoue K, Kondo S, Yoshie Y, et al. Migration of 4-nonylphenol from polyvinyl chloride food packaging films into food simulants and foods. Food Addit Contam 2001;18(2):157-64.

3. Krzymien MIE, Carlsson DJ, Deschnes L, Mercier M. Analyses of volatile transformation products from additives in gamma-irradiated polyethylene packaging. Food Addit Contam 2001;18(8):739-49.

4. Ogata N, Toyoda M, Shibata T. Suppression of intestinal smooth muscle contraction by phenolic compounds. Res Commun Chem Pathol Pharmacol 1992;77(3):359-66.

5. Sakai A. p-Nonylphenol acts as a promoter in the BALB/3T3 cell transformation. Mutat Res 2001;493(l-2): 161-6.

6. Williams K, McKinnel C, Saunders PT, et al. Neonatal exposures to potent and environmental oestrogens and abnormalities of the male reproductive system in the rat: evidence for importance of the androgen-oestrogen balance and assessment of the relevance to man. APMIS Suppl 2001; 103:S493-S504.

7. Yang F, Abdel-Malek Z, Boissy RE. Effects of commonly used mitogens on the cytotoxicity of 4-tertiary butylphenol to human melanocytes. In Vitro Cell Dev Biol Anim 1999;35(10):566-70.

Table 1. Additional Chemicals for the Alkylphenols Category

CAS No.	Chemical	Industry Sponsor
27193868	Phenol, dodecyl-	American Chemistry Council (ACC) Health, Environmental, and Research Task Group (HERTG)
74499357	Phenol, (tetrapropenyl) derivs.	American Chemistry Council (ACC) Health, Environmental, and Research Task Group (HERTG)
108394	Phenol, 3-methyl-	Bayer AG Corporation
25168063	Phenol, isopropyl-	Great Lakes Chemical Corporation
123079	Phenol, p-ethyl-	Laporte Performance Chemicals UK Limited
104438	Phenol, p-dodecyl-	None
1323655	Phenol, dinonyl-	None
25154523	Phenol, nonyl-	None
27193288	Phenol, octyl-	None
34689468	Phenol, methyl-, sodium salt	None
620177	Phenol, m-ethyl-	None
68081867	Phenol, nonyl derivs.	None
90006	Phenol, o-ethyl-	None
99718	Phenol, p-sec-butyl-	None
105679	Phenol, 2,4-dimethyl	None